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Patient Name: 송재진 Gender: Sample ID: N25-226 **Primary Tumor Site:** 2025.09.11 **Collection Date:**

Sample Cancer Type: Lung Cancer

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Relevant Lung Cancer Findings

Gene	Finding		Gene	Finding	
ALK	None detected		NTRK1	None detected	
BRAF	None detected		NTRK2	None detected	
EGFR	None detected		NTRK3	None detected	
ERBB2	None detected		RET	None detected	
KRAS	None detected		ROS1	CD74::ROS1 fusion	
MET	None detected				
Genomic Alt	teration	Finding			
Tumor Mu	utational Burden	3.8 Mut/Mb measured			

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	CD74::ROS1 fusion CD74 molecule - ROS proto-oncogene 1, receptor tyrosine kinase Locus: chr5:149784243 - chr6:117645578	crizotinib 1,2/l, + entrectinib 1,2/l, + repotrectinib 1,2/l, + lorlatinib +	crizotinib ⁺ entrectinib ⁺	35

^{*} Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

Line of therapy: I: First-line therapy, II+: Other line of therapy

Tier Reference: Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23.



🛕 Alerts informed by public data sources: 🧿 Contraindicated, 🏮 Resistance, 🧳 Breakthrough, 🛕 Fast Track

CD74::ROS1 fusion

Public data sources included in alerts: FDA1_NCCN_EMA2_ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources

Microsatellite stable, TP53 p.(G266E) c.797G>A, HLA-B deletion, KLF5 p.(E419Q) c.1255G>C, NQ01 p.(P187S) c.559C>T, Tumor Mutational Burden

^{*} Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

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Variant Details

DNA Sequence Variants Allele Gene **Amino Acid Change** Codina Variant ID Locus Frequency Transcript **Variant Effect** TP53 c.797G>A COSM10867 chr17:7577141 p.(G266E) 26.90% NM 000546.6 missense KLF5 p.(E419Q) c.1255G>C COSM396907 chr13:73649905 24.10% NM_001730.5 missense NQ01 p.(P187S) c.559C>T chr16:69745145 48.87% NM_000903.3 missense **CREBBP** chr16:3779031 46.15% NM_004380.3 p.(N2006S) c 6017A>G missense NOTCH3 p.([P1521=;E1522G]) c.4563_4565delAGAins . chr19:15285050 2.03% NM_000435.3 synonymous, GGG missense U2AF1 p.(I24T) c.71T>C chr21:44524486 18.18% NM_006758.3 missense

Gene Fusions		
Genes	Variant ID	Locus
CD74::ROS1	CD74-ROS1.C6R34.COSF1200.1	chr5:149784243 - chr6:117645578
CD74::ROS1	CD74-ROS1.C6R35.1	chr5:149784243 - chr6:117642557

Copy Number Variations			
Gene	Locus	Copy Number	CNV Ratio
HLA-B	chr6:31322252	0.89	0.56

Biomarker Descriptions

CD74::ROS1 fusion

CD74 molecule, ROS proto-oncogene 1, receptor tyrosine kinase

<u>Background:</u> The ROS1 gene encodes the ROS proto-oncogene receptor tyrosine kinase 1, which exhibits structural similarity to anaplastic lymphoma kinase (ALK)^{10,11}. Like ALK, ROS1 is the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact ROS1 tyrosine kinase domain combined with numerous fusion partner genes¹². ROS1 fusion kinases are constitutively activated and drive oncogenic transformation¹³.

Alterations and prevalence: Somatic mutations in ROS1 are observed in 24% of skin cutaneous melanoma, 13% of uterine corpus endometrial carcinoma, 8% of lung squamous cell carcinoma, 7% of colorectal adenocarcinoma, 6% of stomach adenocarcinoma, 5% of bladder urothelial carcinoma, head and neck squamous cell carcinoma, and diffuse large B-cell lymphoma, 4% of lung adenocarcinoma and uterine carcinosarcoma, 3% of adrenocortical carcinoma, esophageal adenocarcinoma, cholangiocarcinoma, cervical squamous cell carcinoma, kidney renal clear cell carcinoma, and glioblastoma multiforme, and 2% of mesothelioma, brain lower grade glioma, breast invasive carcinoma, and acute myeloid leukemia^{8,9}. ROS1 fusions are observed in cholangiocarcinoma, gastric cancer, and ovarian cancer and have been reported in approximately 1-2% of non-small cell lung cancer (NSCLC) and glioblastoma^{10,14,15,16,17,18}. ROS1 amplification is observed in 3% of sarcoma^{8,9}. Alterations in ROS1 are rare in pediatric cancers^{8,9}. Somatic mutations are observed in 2% of bone cancer and embryonal tumors, and 1% or less in B-lymphoblastic leukemia/lymphoma (3 in 252 cases), glioma (3 in 297 cases), leukemia (1 in 311 cases), peripheral nervous system tumors (3 in 1158 cases), and Wilms tumor (1 in 710 cases)^{8,9}. Amplification of ROS1 is observed in less than 1% of B-lymphoblastic leukemia/lymphoma (1 in 731 cases)^{8,9}.

Potential relevance: The tyrosine kinase inhibitor (TKI), entrectinib¹⁹ (2019), is approved for the treatment of ROS1 fusion-positive metastatic NSCLC. Crizotinib²⁰ (2011), originally approved for the treatment of ALK-positive NSCLC, is also approved (2016) for the treatment of ROS1-positive NSCLC²¹. Acquired resistance to crizotinib in ROS1-positive NSCLC is associated with kinase domain mutations S1986F/Y, G2032R, D2033N, and L2155S^{22,23,24}. Repotrectinib²⁵ (2023) is a kinase inhibitor approved for the treatment of locally advanced or metastatic ROS1-positive NSCLC. In 2024, zidesamtinib²⁶ received breakthrough designation for the treatment of patients with ROS1-positive NSCLC who have been previously treated with two or more ROS1 TKIs. The ROS1 inhibitor, taletrectinib²⁷

Biomarker Descriptions (continued)

(2022), was also granted breakthrough designation for the treatment of adult patients with advanced or metastatic ROS1-positive NSCLC who are ROS1 tyrosine kinase inhibitor (TKI) treatment-naïve or previously treated with crizotinib. Ceritinib²⁸ (2017) is a second-generation ALK inhibitor approved for ALK-positive NSCLC that has also shown efficacy in ROS1-positive NSCLC²⁹. In a phase II study, ceritinib demonstrated systemic and intra-cranial activity with an objective response rate (ORR) of 62% in patients with advanced ROS1-positive NSCLC²⁹. Lorlatinib³⁰, a CNS-penetrant third-generation ALK and ROS1 inhibitor, is FDA approved (2018) for ALK-positive metastatic NSCLC. Emerging pre-clinical evidence suggests that lorlatinib may target almost all known ALK and ROS1 resistance mutations^{31,32}. In a phase I/II study of lorlatinib in advanced ROS1-positive NSCLC, objective responses were observed in both TKI-naïve and those previously treated with crizotinib, regardless of CNS metastasis³³. Lorlatinib is recommended for subsequent therapy in ROS1 fusion-positive NSCLC patients who have progressed after treatment with crizotinib, entrectinib, or ceritinib³⁴.

Microsatellite stable

Background: Microsatellites are short tandem repeats (STR) of 1 to 6 bases of DNA between 5 to 50 repeat units in length. There are approximately 0.5 million STRs that occupy 3% of the human genome⁶¹. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{62,63}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2⁶⁴. Mutations and loss of expression in MMR genes, known as defective MMR (dMMR), lead to MSI. In contrast, when MMR genes lack alterations, they are referred to as MMR proficient (pMMR). Consensus criteria were first described in 1998 and defined MSI-high (MSI-H) as instability in two or more of the following five markers: BAT25, BAT26, D5S346, D2S123, and D17S250⁶⁵. Tumors with instability in one of the five markers were defined as MSI-low (MSI-L) whereas, those with instability in zero markers were defined as MS-stable (MSS)⁶⁵. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{66,67,68,69,70}. MSI-H is a hallmark of Lynch syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in the MMR genes⁶³. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{62,63,67,71}.

Alterations and prevalence: The MSI-H phenotype is observed in 30% of uterine corpus endothelial carcinoma, 20% of stomach adenocarcinoma, 15-20% of colon adenocarcinoma, and 5-10% of rectal adenocarcinoma^{62,63,72,73}. MSI-H is also observed in 5% of adrenal cortical carcinoma and at lower frequencies in other cancers such as esophageal, liver, and ovarian cancers^{72,73}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab⁷⁴ (2014) and nivolumab⁷⁵ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab⁷⁴ is also approved as a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR with disease progression on prior therapy who are not candidates for surgery or radiation. Importantly, pembrolizumab is approved for the treatment of MSI-H or dMMR solid tumors that have progressed following treatment, with no alternative option and is the first anti-PD-1 inhibitor to be approved with a tumor agnostic indication⁷⁴. Dostarlimab⁷⁶ (2021) is also approved for dMMR recurrent or advanced endometrial carcinoma or solid tumors that have progressed on prior treatment and is recommended as a subsequent therapy option in dMMR/MSI-H advanced or metastatic colon or rectal cancer^{68,77}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab⁷⁸ (2011), is approved alone or in combination with nivolumab in MSI-H or dMMR colorectal cancer that has progressed following treatment with chemotherapy. MSI-H may confer a favorable prognosis in colorectal cancer although outcomes vary depending on stage and tumor location^{68,79,80}. Specifically, MSI-H is a strong prognostic indicator of better overall survival (OS) and relapse free survival (RFS) in stage II as compared to stage III colorectal cancer patients⁸⁰. The majority of patients with tumors classified as either MSS or pMMR do not benefit from treatment with single-agent immune checkpoint inhibitors as compared to those with MSI-H tumors^{81,82}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{81,82}.

TP53 p.(G266E) c.797G>A

tumor protein p53

Background: The TP53 gene encodes the tumor suppressor protein p53, which binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair¹. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis³⁵. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential³⁶. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers^{37,38}.

Alterations and prevalence: TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)^{8,9,39,40,41,42}. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common, including substitutions at codons R158, R175, Y220, R248, R273, and R282^{8,9}. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes^{43,44,45,46}. Alterations in TP53 are also observed in pediatric cancers^{8,9}. Somatic mutations are observed in 53% of non-Hodgkin lymphoma, 24% of soft tissue sarcoma, 19%

Biomarker Descriptions (continued)

of glioma, 13% of bone cancer, 9% of B-lymphoblastic leukemia/lymphoma, 4% of embryonal tumors, 3% of Wilms tumor and leukemia, 2% of T-lymphoblastic leukemia/lymphoma, and less than 1% of peripheral nervous system cancers (5 in 1158 cases) 8,9. Biallelic loss of TP53 is observed in 10% of bone cancer, 2% of Wilms tumor, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases) and leukemia (1 in 250 cases) 8,9.

Potential relevance: The small molecule p53 reactivator, PC14586⁴⁷ (2020), received a fast track designation by the FDA for advanced tumors harboring a TP53 Y220C mutation. The FDA has granted fast track designation to the p53 reactivator, eprenetapopt⁴⁸, (2019) and breakthrough designation⁴⁹ (2020) in combination with azacitidine or azacitidine and venetoclax for acute myeloid leukemia patients (AML) and myelodysplastic syndrome (MDS) harboring a TP53 mutation, respectively. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation^{50,51}. TP53 mutation are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma⁵². TP53 mutations confer poor prognosis and poor risk in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL), and acute lymphoblastic leukemia (ALL)^{53,54,55,56,57,58}. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant⁵⁹. Mono- and bi-allelic mutations in TP53 confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occurring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system⁶⁰.

HLA-B deletion

major histocompatibility complex, class I, B

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B1. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells². MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M³. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the α polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self^{4,5,6}. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B⁷.

Alterations and prevalence: Somatic mutations in HLA-B are observed in 10% of diffuse large B-cell lymphoma (DLBCL), 5% of cervical squamous cell carcinoma and stomach adenocarcinoma, 4% of head and neck squamous cell carcinoma and colorectal adenocarcinoma, 3% of uterine cancer, and 2% of esophageal adenocarcinoma and skin cutaneous melanoma^{8,9}. Biallelic loss of HLA-B is observed in 5% of DLBCL^{8,9}.

Potential relevance: Currently, no therapies are approved for HLA-B aberrations.

KLF5 p.(E419Q) c.1255G>C

Kruppel like factor 5

Background: The KLF5 gene encodes the Kruppel like factor 5 protein, a member of the Kruppel-like factor (KLF) subfamily of zinc finger transcription factors within group 2, along with KLF1, KLF2, KLF4, KLF7, and KLF6^{1,83}. KLF proteins are known for their role in the reprogramming of somatic cells into inducible pluripotent stem cells and impact several biological processes including the regulation of proliferation, differentiation, and apoptosis⁸³. KLF5 regulates a variety of target genes including PDGFa, cyclin D1, p21, and p27, and is known to contribute to the regulation of cell proliferation, differentiation, angiogenesis, and migration^{84,85}.

Alterations and prevalence: Somatic mutations in KLF5 are observed in 5% of bladder urothelial carcinoma, 3% of cervical squamous cell carcinoma, 2% of lung squamous cell carcinoma, uterine corpus endometrial carcinoma, and uterine carcinosarcoma^{8,9}. Amplifications in KLF5 are observed in 4% of stomach adenocarcinoma and uterine carcinosarcoma, and 3% of bladder urothelial carcinoma, esophageal adenocarcinoma, head and neck squamous cell carcinoma, and colorectal adenocarcinoma^{8,9}.

Potential relevance: Currently, no therapies are approved for KLF5 aberrations.

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Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated

Not recommended



Resistance Breakthrough



Fast Track

FDA information is current as of 2025-05-14. For the most up-to-date information, search www.fda.gov.

CD74::ROS1 fusion

taletrectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ROS1 fusion

Supporting Statement:

The FDA has granted Breakthrough Therapy designation (BTD) to the ROS-1 inhibitor, taletrectinib, for the treatment of adult patients with advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) who have not been previously treated with ROS1 tyrosine kinase inhibitors or crizotinib.

Reference:

https://www.anhearttherapeutics.com/news/press-releases/080322/

zidesamtinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ROS1 fusion

Supporting Statement:

The FDA has granted Breakthrough Therapy designation to the brain-penetrant ROS1-selective tyrosine kinase inhibitor (TKI), zidesamtinib (NVL-520), for the treatment of patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC) who have been previously treated with two or more ROS1 TKIs.

Reference:

https://investors.nuvalent.com/2024-02-27-Nuvalent-Receives-U-S-FDA-Breakthrough-Therapy-Designation-for-NVL-520

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4, IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLC01B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XP01, ZNF217, ZNF429

Genes Assayed for the Detection of Copy Number Variations

ABCB1, ABL1, ABL2, ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AKT1, AKT2, AKT3, ALK, AMER1, APC, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL2, BCL2L12, BCL6, BCOR, BLM, BMPR2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHD4, CHEK1, CHEK2, CIC, CREBBP, CSMD3, CTCF, CTLA4, CTNND2, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, DAXX, DDR1, DDR2, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, EGFR, EIF1AX, ELF3, EMSY, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERBB2, ERBB3, ERBB4, ERCC2, ERCC4,

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Genes Assayed (continued)

Genes Assayed for the Detection of Copy Number Variations (continued)

ERRFI1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCI, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF3, FGF4, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, F0XA1, FUBP1, FYN, GATA2, GATA3, GLI3, GNA13, GNAS, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, IDH2, IGF1R, IKBKB, IL7R, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF5, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, LARP4B, LATS1, LATS2, MAGOH, MAP2K1, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK1, MAPK8, MAX, MCL1, MDM2, MDM4, MECOM, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLH3, MPL, MRE11, MSH2, MSH3, MSH6, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, NBN, NCOR1, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK3, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDIA3, PGD, PHF6, PIK3C2B, PIK3CA, PIK3CA, PIK3CB, PIK3R1, PIK3R2, PIM1, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLCO1B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFHX3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, FGR, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSPO2, RSPO3, TERT

Genes Assayed with Full Exon Coverage

ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AMER1, APC, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AXIN1, AXIN2, B2M, BAP1, BARD1, BCOR, BLM, BMPR2, BRCA1, BRCA2, BRIP1, CALR, CASP8, CBFB, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERRF11, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCE, FANCG, FANCI, FANCI, FANCH, FA

Relevant Therapy Summary

In this cancer type	O In other cancer type	In this cancer type and other cancer types		✗ No evidence		
CD74::ROS1 fus	sion					
Relevant Therapy		FDA	NCCN	EMA	ESMO	Clinical Trials*
entrectinib			•			(II/III)
crizotinib			•			(II)
repotrectinib		•	•	•	•	(II)
lorlatinib		×	•	×	×	×

^{*} Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

In this cancer type

O In other cancer type

In this cancer type and other cancer types

X No evidence

CD74::ROS1 fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
entrectinib, crizotinib	×	×	×	×	(III)
repotrectinib, crizotinib	×	×	×	×	(III)
sacituzumab tirumotecan	×	×	×	×	(III)
taletrectinib, crizotinib	×	×	×	×	(III)
targeted therapy	×	×	×	×	(III)
cabozantinib	×	×	×	×	(II)
ceritinib	×	×	×	×	(II)
ICP-723	×	×	×	×	(II)
sacituzumab govitecan	×	×	×	×	(II)
amivantamab, lorlatinib, entrectinib	×	×	×	×	(I/II)
benmelstobart, catequentinib	×	×	×	×	(I/II)
furetinib	×	×	×	×	(I/II)
XZP-5955	×	×	×	×	(I/II)
zidesamtinib	×	×	×	×	(I/II)
APG-2449	×	×	×	×	(I)
HG 030	×	×	×	×	(1)
JYP-0322	×	×	×	×	(I)
LZ-001	×	×	×	×	(I)
talazoparib, crizotinib	×	×	×	×	(I)

^{*} Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

HRR Details

Gene/Genomic Alteration	Finding
Not Detected	Not Applicable

Homologous recombination repair (HRR) genes were defined from published evidence in relevant therapies, clinical guidelines, as well as clinical trials, and include - BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L.

Thermo Fisher Scientific's lon Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.1.1 data version 2025.06(006)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-05-14. NCCN information was sourced from www.nccn.org and is current as of 2025-05-01. EMA information was sourced from www.ema.europa.eu and is current as of 2025-05-14. ESMO information was sourced from www.esmo.org and is current as of 2025-05-01. Clinical Trials information is current as of 2025-05-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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